

Abstract

A method for engineering and utilizing large DNA vectors to target, via
5 homologous recombination, and modify, in any desirable fashion,
endogenous genes and chromosomal loci in eukaryotic cells. These large
DNA targeting vectors for eukaryotic cells, termed LTVECs, are derived
from fragments of cloned genomic DNA larger than those typically used by
other approaches intended to perform homologous targeting in eukaryotic
10 cells. Also provided is a rapid and convenient method of detecting
eukaryotic cells in which the LTVEC has correctly targeted and modified
the desired endogenous gene(s) or chromosomal locus (loci) as well as the
use of these cells to generate organisms bearing the genetic modification.